Annals of Internal Medicine

CLINICAL GUIDELINE

The Management of Chronic Insomnia Disorder and Obstructive Sleep Apnea: Synopsis of the 2019 U.S. Department of Veterans Affairs and U.S. Department of Defense Clinical Practice Guidelines

Vincent Mysliwiec, MD; Jennifer L. Martin, PhD; Christi S. Ulmer, PhD, DBSM; Susmita Chowdhuri, MD, MS; Matthew S. Brock, MD; Christopher Spevak, MD, MPH, JD; and James Sall, PhD

Description: In September 2019, the U.S. Department of Veterans Affairs (VA) and the U.S. Department of Defense (DoD) approved a new joint clinical practice guideline for assessing and managing patients with chronic insomnia disorder and obstructive sleep apnea (OSA). This guideline is intended to give health care teams a framework by which to screen, evaluate, treat, and manage the individual needs and preferences of VA and DoD patients with either of these conditions.

Methods: In October 2017, the VA/DoD Evidence-Based Practice Work Group initiated a joint VA/DoD guideline development effort that included clinical stakeholders and conformed to the Institute of Medicine's tenets for trustworthy clinical practice guidelines. The guideline panel developed key questions, systematically searched and evaluated the literature, created three 1-page algorithms, and advanced 41 recommendations using the GRADE (Grading of Recommendations Assessment, Development and Evaluation) system.

Recommendations: This synopsis summarizes the key recommendations of the guideline in 3 areas: diagnosis and assessment of OSA and chronic insomnia disorder, treatment and management of OSA, and treatment and management of chronic insomnia disorder. Three clinical practice algorithms are also included.

Ann Intern Med. doi:10.7326/M19-3575 **Annals.org**

This article was published at Annals.org on 18 February 2020.

For author affiliations, see end of text.

The National Institutes of Health has estimated that insomnia and obstructive sleep apnea (OSA) are 2 of the most common sleep disorders in the general U.S. population and in the military and veteran populations (1). Insomnia symptoms are the most common sleep symptoms among U.S. adults, occurring in approximately 20% to 30% of adults, and the prevalence of chronic insomnia disorder ranges from 6% to 10% (2–6). The prevalence of OSA ranges from 9% to 38% and is associated with older age, higher body mass index, male sex, and menopause.

Sleep disorders are more prevalent in the populations served by the U.S. Department of Veterans Affairs (VA) and the U.S. Department of Defense (DoD) than in the general civilian population. In the RAND report "Sleep in the Military: Promoting Healthy Sleep Among U.S. Servicemembers," 48.6% of military personnel surveyed had poor sleep quality (Pittsburgh Sleep Quality Index score >5) (7). The prevalence of insomnia symptoms has been reported to be as high as 41% in service members deployed to combat and 25% in noncombatants (8). In a large cohort of soldiers preparing for deployment, 19.9% met criteria for insomnia according to the Insomnia Severity Index (ISI) (8). A more recent study evaluated the incidence of insomnia and OSA in the entire population of U.S. Army soldiers from 1997 to 2011 (9) and showed unprecedented increases in the incidence of both conditions (652% and 600%, respectively) during this period. In military personnel referred for sleep evaluations, sleep-disordered breathing is the most frequently diagnosed disorder, and some studies have found that military personnel have high rates of comorbid insomnia and OSA (10, 11). Further, military personnel with sleep disorders often also have posttraumatic stress disorder (PTSD), symptoms of anxiety and depression, and traumatic brain injury, which can complicate diagnosis and management (11–13).

Sleep disturbances are also common in veterans (14–16). Similar to findings from active-duty service members, the National Veteran Sleep Disorder Study found that the number of veterans diagnosed with sleep disorders increased nearly 6-fold from 2000 to 2010. In this study, 4.5% of veterans were diagnosed with sleep-disordered breathing, and 2.5% were diagnosed with insomnia. However, the actual prevalence of insomnia disorder among veterans is likely to be considerably higher (17) because it is often not documented in the medical record (18, 19). Comorbid PTSD was associated with a 7.6-fold greater risk for OSA and a 6.3-fold greater risk for insomnia (15). Because veterans have high rates of cardiovascular disease and PTSD, and because OSA is more prevalent in patients with these disorders (20), there is likely a large percentage of veterans who have not yet been diagnosed with OSA (21).

See also:

Web-Only
CME/MOC activity

GUIDELINE DEVELOPMENT PROCESS

To develop these recommendations, the VA/DoD followed a process developed by the VA/DoD Evidence-Based Practice Work Group that adheres to the standards for trustworthy guidelines (22). The group selected 4 guideline panel cochairs, 2 from the VA and 2 from the DoD. The cochairs, in conjunction with VA and DoD leadership, selected a multidisciplinary panel of practicing clinician stakeholders from various specialties, including sleep medicine, neurology, psychology, psychiatry, pulmonology, otolaryngology, internal medicine, dentistry, pharmacy, and nursing. The VA/DoD contracted with The Lewin Group, a third party with expertise in clinical practice guideline development, to facilitate meetings and the development of key questions using the PICOTS (population, intervention, comparator, outcomes, timing of outcomes measurement, and setting) format. A patient and family stakeholder focus group was convened to assist in determining the scope and inform the development of key questions. The guideline panel developed 20 key questions to guide the evidence review. The systematic search of the peer-reviewed literature was conducted by ECRI Institute and covered the period from 1 January 2008 to 15 May 2018. The search methods and results are detailed in the full guideline (www.healthquality.va.gov/guidelines/CD/insomnia/index.asp). In collaboration with ECRI Institute, the guideline panel evaluated the body of evidence and developed the recommendations using the GRADE (Grading of Recommendations Assessment, Development and Evaluation) methods (23–25).

RECOMMENDATIONS

This guideline represents an important step toward improving the management of patients with chronic insomnia disorder, OSA, or both in the VA and DoD. As with other clinical practice guidelines, challenges remain, including evidence gaps and the need to develop effective strategies for guideline implementation and for evaluation of the effect of guideline adherence on clinical outcomes. This guideline is intended for VA and DoD health care practitioners, including physicians, nurse practitioners, physician assistants, psychologists, social workers, nurses, clinical pharmacy specialists, dental specialists, and others involved in the care of service members or veterans with chronic insomnia disorder, OSA, or both.

Diagnosis and Assessment of OSA and Chronic Insomnia Disorder

Assessment of patients with sleep symptoms is the first step in identification of OSA, and evidence supports use of specific screening questionnaires. With an apnea–hypopnea index (AHI) of 5 events per hour or greater on polysomnography (PSG) as the gold standard to define OSA, our evidence review yielded data on the diagnostic accuracy of the Berlin Questionnaire, the STOP questionnaire, the STOP-BANG questionnaire, and the Epworth Sleepiness Scale (26).

After reviewing the sensitivity and specificity of each tool reported by Chiu and colleagues (26), the work group agreed that none had acceptable accuracy to definitively diagnose OSA. Because objective testing is required after screening, the work group focused on sensitivity as the metric of choice to increase the likelihood of detecting OSA on diagnostic testing. Among the 4 screening tools, STOP and STOP-BANG had the highest sensitivities. Given the performance similarities and simpler administration, the STOP questionnaire was included in our recommendation. This questionnaire consists of 4 dichotomous (yes or no) questions on snoring; tiredness, fatigue, or sleepiness during the daytime; observed apnea episodes; and history of high blood pressure. A score of 2 or higher (out of a possible 4, with 1 point for each positive response) discriminates high from low risk for OSA (27).

Although in-laboratory PSG is the gold standard for diagnosis of OSA, home sleep apnea testing (HSAT) is increasingly performed in clinical practice to establish the diagnosis among patients with a high pretest probability (28). Evidence supports use of a manually scored type III HSAT (unattended portable monitor) and an event index (for example, respiratory disturbance index, respiratory event index, or AHI) of 15 events per hour or higher to establish a diagnosis of moderate to severe OSA (29); however, the evidence is less clear for mild OSA (respiratory event index of 5 to 15 events per hour). For patients who have nondiagnostic HSAT (technically inadequate or AHI <5 events per hour), repeated testing with either HSAT or in-laboratory PSG should be done (29). In patients with an uncertain diagnosis of OSA or for whom treatment proves challenging, consultation with a sleep specialist is recommended.

In patients with suspected chronic insomnia disorder, self-reported measures are an important part of a comprehensive assessment. The ISI and the Athens Insomnia Scale are 2 such measures that have high diagnostic accuracy for insomnia (30). A systematic review found that both were sensitive and specific for accurately distinguishing between patients with and without insomnia disorder (31). A formal diagnosis of chronic insomnia disorder requires a detailed sleep, medical, substance, and psychiatric history.

Treatment and Management of OSA

For treatment of OSA, the work group recommended positive airway pressure (PAP) therapy for the entirety of a person's sleep period. Because adherence can be challenging, the work group also suggested continuing PAP treatment for OSA even in patients using it for less than 4 hours per night (the Medicare standard) and providing supportive, educational, and behavioral interventions to improve adherence early in treatment (32). Alcohol and certain medications (such as opioids or sedative hypnotics) can worsen OSA in some patients and should be used with caution or avoided if possible.

The literature supports an association between greater PAP use and improved outcomes, although there is no definitive evidence that it prevents major

adverse cardiovascular events (29, 33–35). Barbé and colleagues found no differences in the intention-to-treat comparison of PAP versus control, whereby patients received no active intervention. However, PAP use for 4 or more hours per night was associated with reduced risk for new-onset hypertension or cardiovascular events compared with controls (7.90 vs. 11.02 events per 100 person-years) (29). In a meta-analysis of 235 studies, Khan and colleagues reported a clinically nonsignificant 26% risk reduction in major adverse cardiovascular events with mean PAP use of 3.5 hours per night; however, a sensitivity analysis found that increased use was associated with a decrease in major adverse cardiovascular events that was primarily driven by a clinically significant decrease in stroke (33). In addition, several studies have reported benefits for health-related quality of life with PAP use for less than 4 hours per night. For example, the BestAIR (Best Apnea Interventions for Research) study found that PAP therapy in patients with moderate to severe OSA without severe sleepiness improved several domains of health-related quality of life as well as daytime sleepiness (34), even though mean use was 3.8 hours per night at 6 months and 3.4 hours per night at 12 months. The safety of PAP therapy has been established across multiple cohort and interventional studies, and it is associated with primarily mild adverse effects, including nasal congestion, oronasal dryness, mask discomfort, and nocturnal awakenings (35).

After PAP therapy, the next most-studied treatments for OSA are mandibular advancement devices (MADs). The work group specifically reviewed studies comparing PAP therapy and MADs for patients with mild to moderate OSA (36–40). Although all studies concluded that PAP therapy was superior in reducing AHI, none found a statistically significant difference in improvement of daytime sleepiness, cognitive function, vigilance, hypertension, or quality-of-life measures. One randomized crossover trial of veterans diagnosed with OSA and PTSD reported clinically significant greater patient preference and adherence to MADs over PAP therapy (36), with an equivalent amelioration of PTSD and sleep-related quality-of-life symptoms. Thus, although MADs may not be as efficacious as PAP therapy in reducing AHI, their increased use, due in part to patient preference and acceptance, may result in similar overall treatment benefits.

Treatment and Management of Chronic Insomnia Disorder

Cognitive and Behavioral Interventions

Evidence suggests that cognitive behavioral therapy for insomnia (CBT-I) is effective in treating chronic insomnia. This therapy is a multisession, multicomponent treatment focused on sleep-specific thoughts and behaviors. Behavioral components include sleep restriction therapy (limiting time in bed to sleep time, followed by a gradual increase in time in bed as sleep efficiency improves), stimulus control (strengthening the association between the sleep environment and sleep and establishing consistent sleep patterns), relaxation therapy and counterarousal strategies, and sleep hygiene education (41, 42). Cognitive therapy components target maladaptive thoughts and beliefs about sleep. An abbreviated version of CBT-I, brief behavioral treatment for insomnia (BBT-I), focuses on the behavioral components of sleep restriction, stimulus control, and sleep hygiene only. Two systematic reviews examined the efficacy of behavioral therapies for insomnia. Trials assessed outcomes in the general adult population, subpopulations of older adults (for example, those aged ≥55 years), and patients with comorbid pain (41, 43). The systematic review by Brasure and colleagues (41) included 59 trials comparing CBT-I and BBT-I with passive controls and reported outcomes favoring these treatments, including improvements in ISI scores, sleep efficiency, sleep quality, and wake time after sleep onset (41).

The work group also considered delivery methods for CBT-I. Telehealth delivery platforms included provider-directed telemedicine and self-directed Internet-based programs that have been studied in patients with chronic insomnia, and these are potential strategies for increasing access to CBT-I in VA and DoD populations (44–48). Ultimately, the group concluded that the evidence was insufficient to recommend for or against use of Internet-based or group delivery of CBT-I compared with face-to-face treatment.

Sleep hygiene education and pharmacotherapy are the most commonly offered treatments for chronic insomnia disorder (18); however, the work group concluded that these should not be considered first-line therapies (see the next 2 paragraphs). Sleep hygiene education commonly includes information about caffeine, alcohol, and nicotine use; exercise; the sleep environment; sleep–wake regularity and nap avoidance; and stress management (49). Although sleep hygiene education is a component of CBT-I, the work group evaluated the evidence for it as a standalone treatment. A systematic review by Chung and colleagues (49) included 12 studies that compared sleep hygiene education as monotherapy versus CBT-I for treatment of poor sleep or insomnia. None of the studies that were reviewed compared sleep hygiene education with no treatment or usual care, and findings favored CBT-I over sleep hygiene education for sleep onset latency, wake after sleep onset, sleep efficiency, and Pittsburgh Sleep Quality Index and ISI scores (49). In addition, a randomized controlled trial (RCT) by Morgan and colleagues (50) compared self-help CBT-I (for example, 6 weekly booklets that provided information on components of CBT-I) with advice on sleep hygiene. The self-help group showed clinically significant improvements in insomnia severity, sleep efficiency, and sleep quality (50).

Although the work group acknowledged a role of sleep hygiene education as a way to promote healthy sleep practices and prevent poor sleep habits among patients without chronic insomnia disorder, it concluded that sleep hygiene education alone may be not only ineffectual but also potentially harmful if patients receiving it as treatment for chronic insomnia disorder

Table. Recommendations

Recommendations, by Topic	Strength*	Category†
Diagnosis and assessment of OSA and insomnia disorder		
1. For patients who report sleep symptoms, we suggest using the STOP questionnaire to stratify risk for OSA.	Weak for	Reviewed, newly added
2. We suggest that providers assess for sleep-disordered breathing in patients with a history of cardiovascular or cerebrovascular events, congestive heart failure, and long-term prescription opioid use.	Weak for	Reviewed, newly added
3. Among patients with a high pretest probability of OSA, we suggest a manually scored type III home sleep apnea test (unattended portable monitor) using an event index (e.g., respiratory disturbance index, apnea–hypopnea index) ≥15 events per hour to establish the diagnosis of moderate to severe OSA.	Weak for	Reviewed, newly added
4. For patients with a high pretest probability of OSA and a nondiagnostic home sleep apnea test (i.e., technically inadequate or apnea–hypopnea index <5 events per hour), we recommend repeated testing (home sleep apnea testing or laboratory-based polysomnography) for OSA.	Strong for	Reviewed, newly added
5. For evaluating patients with suspected insomnia disorder, we suggest using the Insomnia Severity Index or the Athens Insomnia Scale as part of a comprehensive sleep assessment.	Weak for	Reviewed, newly added
6. There is no available evidence to recommend for or against additional diagnostic testing for patients with chronic insomnia disorder who do not respond to CBT-I or pharmacotherapy.	Neither for nor against	Reviewed, newly added
Treatment and management of OSA		
7. We recommend that patients with OSA receiving PAP therapy use this treatment for the entirety of their sleep periods.	Strong for	Reviewed, newly added
8. We suggest continuing PAP therapy for patients with OSA even if the patient is using it for <4 hours per night.	Weak for	Reviewed, newly added
9. In patients with OSA, including those at high risk for poor adherence to PAP therapy (such as those with posttraumatic stress disorder, anxiety, or insomnia), we recommend educational, behavioral, and supportive interventions to improve PAP adherence.	Strong for	Reviewed, newly added
10. We suggest that patients with OSA and concurrent diagnoses/symptoms of posttraumatic stress disorder, anxiety, or insomnia be offered interventions to improve PAP adherence on initiation of therapy.	Weak for	Reviewed, newly added
11. In appropriate patients with mild to moderate OSA (apnea–hypopnea index <30 events per hour), we suggest offering mandibular advancement devices, fabricated by a qualified dental provider, as an alternative to PAP therapy.	Weak for	Reviewed, newly added
12. Among patients with anatomical nasal obstruction as a barrier to PAP use, we suggest evaluation for nasal surgery.	Weak for	Reviewed, newly added
13. For patients with OSA with an apnea–hypopnea index of 15–65 events per hour and a body mass index <32 kg/m^2 who cannot adhere to PAP therapy, we suggest evaluation for surgical treatment with hypoglossal nerve stimulation therapy.	Weak for	Reviewed, newly added
14. For patients with severe OSA who cannot tolerate or are not appropriate candidates for other recommended therapies, we suggest evaluation for alternative treatment with maxillomandibular advancement surgery.	Weak for	Reviewed, newly added
15. For patients with OSA who cannot tolerate or have declined all other recommended treatments, we suggest offering alternative/salvage therapies.	Weak for	Reviewed, newly added
16. We suggest against oxygen therapy as a standalone treatment for patients with OSA who cannot tolerate other recommended therapies.	Weak against	Reviewed, newly added
17. For patients without nasal congestion, we suggest against routine use of topical nasal steroids for the sole purpose of improving PAP adherence.	Weak against	Reviewed, newly added
18. Due to the lack of clinically significant benefit, we cannot recommend for or against 1) autotitrating PAP compared with fixed PAP, or 2) use of flexible pressure delivery (e.g., C-Flex [Respironics], expiratory pressure relief) to improve PAP adherence.	Neither for nor against	Reviewed, newly added
Treatment and management of chronic insomnia disorder		
Behavioral and psychological treatments		
19. We recommend offering CBT-I for treatment of chronic insomnia disorder.	Strong for	Reviewed, newly added
20. We suggest offering BBT-I for treatment of chronic insomnia disorder.	Weak for	Reviewed, newly added
21. There is insufficient evidence to recommend for or against group vs. individual CBT-I for treatment of chronic insomnia disorder.	Neither for nor against	Reviewed, newly added
22. There is insufficient evidence to recommend for or against Internet-based CBT-I as an alternative to face-to-face CBT-I for treatment of chronic insomnia disorder.	Neither for nor against	Reviewed, newly added
23. For patients diagnosed with chronic insomnia disorder, we suggest CBT-I over pharmacotherapy as first-line treatment.	Weak for	Reviewed, newly added
24. We suggest offering CBT-I for treatment of chronic insomnia disorder that is comorbid with another psychiatric disorder.	Weak for	Reviewed, newly added
25. There is insufficient evidence to recommend for or against mindfulness meditation for treatment of chronic insomnia disorder.	Neither for nor against	Reviewed, newly added
26. We suggest against sleep hygiene education as a standalone treatment for chronic insomnia disorder.	Weak against	Reviewed, newly added

Continued on following page

Table–Continued

Recommendations, by Topic	Strength*	Category†
Complementary and integrative health treatments		
27. We suggest offering auricular acupuncture with seed and pellet for treatment of chronic insomnia disorder.	Weak for	Reviewed, newly added
28. There is insufficient evidence to recommend for or against acupuncture other than auricular acupuncture with seed and pellet for treatment of chronic insomnia disorder.	Neither for nor against	Reviewed, newly added
29. There is insufficient evidence to recommend for or against aerobic exercise, resistive exercise, tai chi, yoga, and qigong for treatment of chronic insomnia disorder.	Neither for nor against	Reviewed, newly added
30. We suggest against cranial electrical stimulation for treatment of chronic insomnia disorder.	Weak against	Reviewed, newly added
Over-the-counter treatments		
31. We suggest against use of diphenhydramine for treatment of chronic insomnia disorder.	Weak against	Reviewed, newly added
32. We suggest against use of melatonin for treatment of chronic insomnia disorder.	Weak against	Reviewed, newly added
33. We suggest against use of valerian and chamomile for treatment of chronic insomnia disorder.	Weak against	Reviewed, newly added
34. We recommend against use of kava for treatment of chronic insomnia disorder.	Strong against	Reviewed, newly added
Pharmacotherapy		
35. In patients who are offered short-course pharmacotherapy for treatment of chronic insomnia disorder, we suggest use of low-dose (i.e., 3 or 6 mg) doxepin.	Weak for	Reviewed, newly added
36. In patients who are offered short-course pharmacotherapy for treatment of chronic insomnia disorder, we suggest use of a nonbenzodiazepine benzodiazepine receptor agonist.	Weak for	Reviewed, newly added
37. There is insufficient evidence to recommend for or against use of ramelteon for treatment of chronic insomnia disorder.	Neither for nor against	Reviewed, newly added
38. There is insufficient evidence to recommend for or against use of suvorexant for treatment of chronic insomnia disorder.	Neither for nor against	Reviewed, newly added
39. We suggest against use of antipsychotic drugs for treatment of chronic insomnia disorder.	Weak against	Reviewed, newly added
40. We suggest against use of benzodiazepines for treatment of chronic insomnia disorder.	Weak against	Reviewed, newly added
41. We suggest against use of trazodone for treatment of chronic insomnia disorder.	Weak against	Reviewed, newly added

BBT-I = brief behavioral therapy for insomnia; CBT-I = cognitive behavioral therapy for insomnia; OSA = obstructive sleep apnea; PAP = positive airway pressure.
* For additional information, refer to the Grading Recommendations (page 90 in the guideline).
† For additional information, refer to the Recommendation Categorization (pages 94–95 in the guideline).

are less receptive to referral for effective behavioral treatments, such as CBT-I or BBT-I, in the belief that they also will be ineffectual.

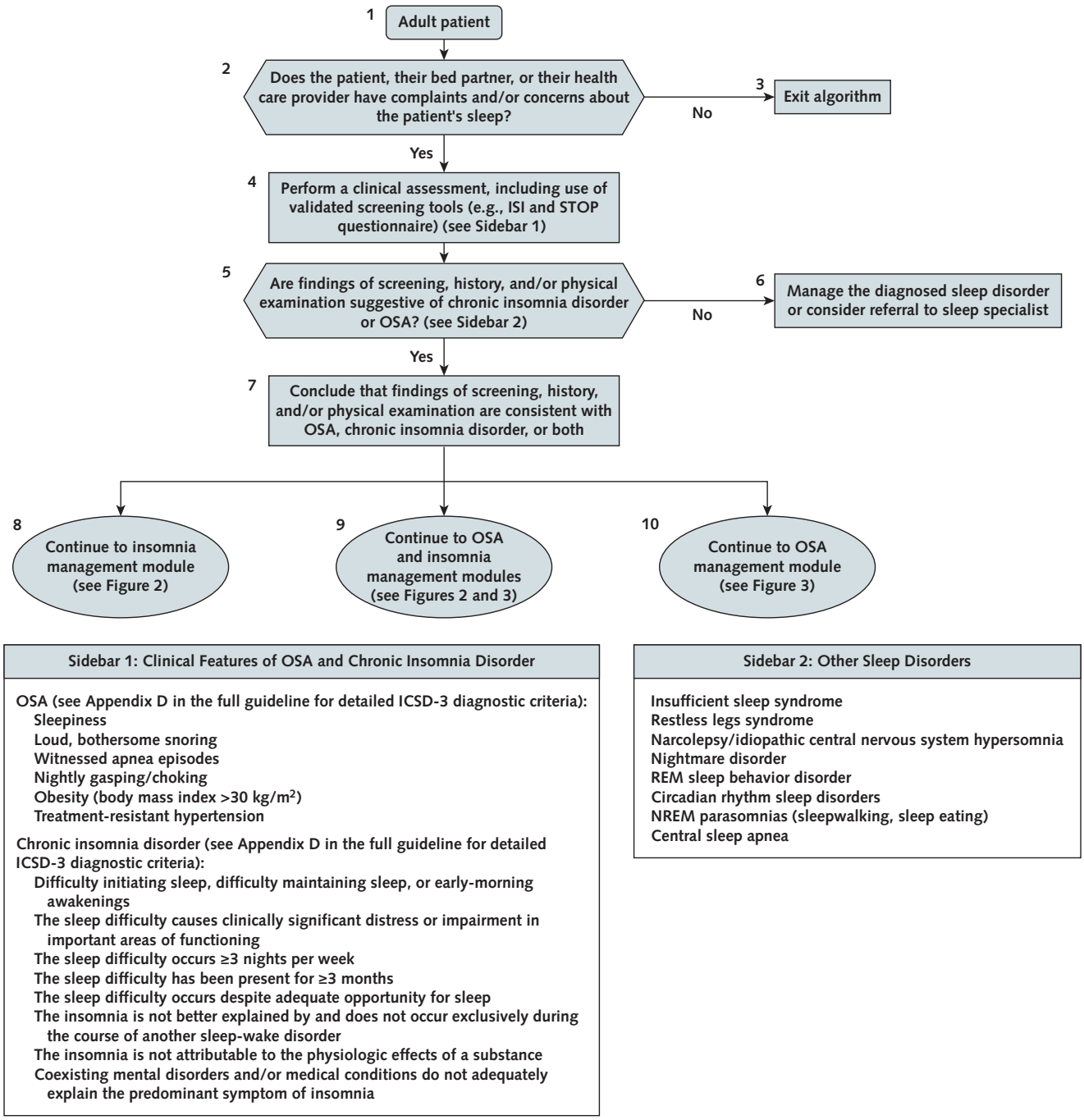
A systematic review by Mitchell and colleagues found that CBT-I was more effective than several pharmacotherapies (51). Compared with pharmacotherapy for chronic insomnia disorder, CBT-I seemed equivalent in short-term results (2 to 4 weeks) but was superior in long-term outcomes. The potential benefits of CBT-I outweigh the potential harms and burden of pharmacotherapy given that there are fewer adverse effects. Of note, there is a lack of clear harms data for pharmacologic treatments beyond relatively brief treatment periods, which raises concerns about potential increased risks with longer courses of pharmacotherapy. In contrast, there are lesser concerns about harms associated with CBT-I given that treatment-related symptoms (sleepiness during the initial phase of sleep restriction therapy) resolve quickly as treatment continues.

Pharmacotherapy

The work group recognized that nonpharmacologic behavioral interventions are more effective than pharmacologic therapies for treatment of chronic insomnia disorder. However, in patients who are unable or unwilling to receive CBT-I, the work group considered offering a short course of low-dose (3 or 6 mg) doxepin or nonbenzodiazepine benzodiazepine receptor agonists (BZRAs) to appropriate candidates. In a low-quality systematic review that included 6 industry-sponsored RCTs, the efficacy of low-dose doxepin (1, 3, and 6 mg) was compared with placebo in persons diagnosed with insomnia disorder (52). Scores on the ISI were improved at week 4 in 2 RCTs in older adults, with the 3- or 6-mg dose of doxepin favored over placebo; effects varied with the 1-mg dose. Subjective sleep latency, total sleep time, and sleep quality outcomes were improved with the 3- and 6-mg doses in older adults in 1 study. These outcomes were also improved in younger adults with the 6-mg dose. None of the RCTs found statistically significant differences in adverse event rates between low-dose doxepin and placebo, although the incidence of adverse events seemed to increase with longer treatment. Low-dose doxepin has no black box warning for suicide risk, but the risk for suicidal ideation associated with use of low-dose doxepin as a hypnotic agent is unknown and cannot be excluded.

A systematic review found that nonbenzodiazepine BZRAs improved the critical outcome of sleep efficiency

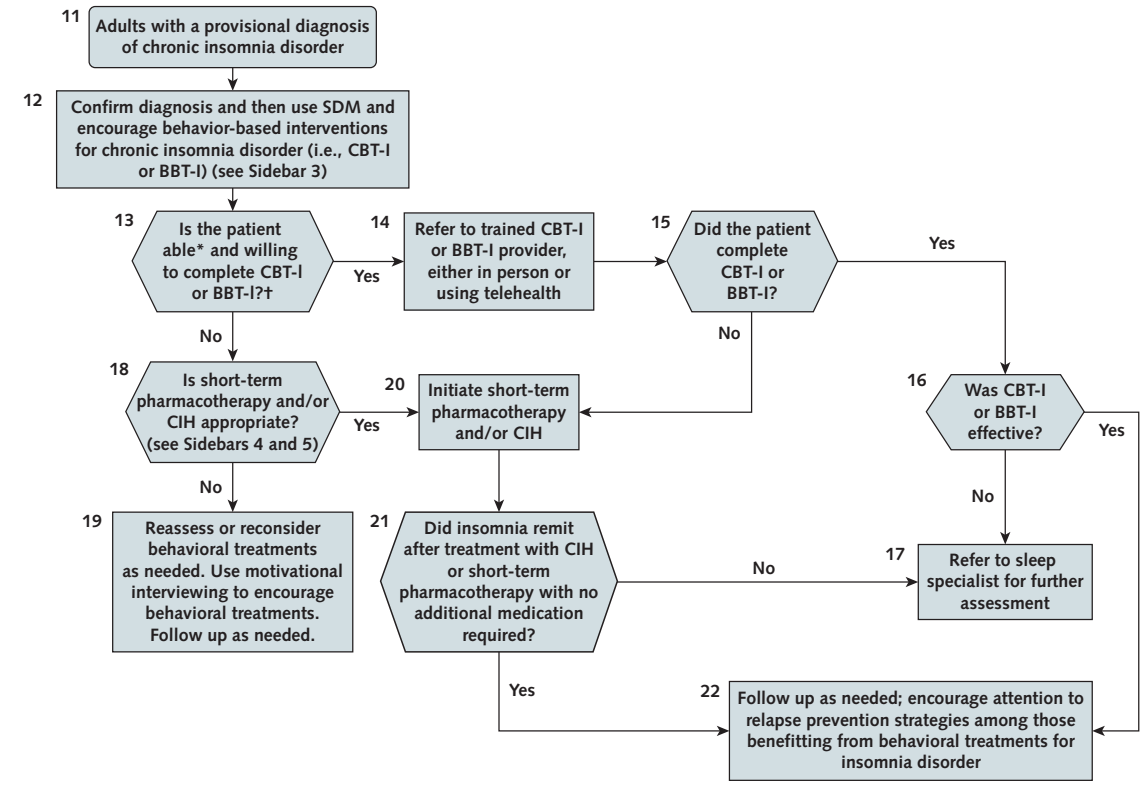
Figure 1. Module A: screening for sleep disorders.



ICSD-3 = International Classification of Sleep Disorders, Third Edition; ISI = Insomnia Severity Index; NREM = non-rapid eye movement; OSA = obstructive sleep apnea; REM = rapid eye movement.

and the important outcomes of sleep onset latency, sleep quality, total sleep time, and wake after sleep onset compared with placebo (53). This review included 17 RCTs studying the efficacy of different formulations, doses, and frequency of administration of 4 nonbenzodiazepine BZRAs: zolpidem, zaleplon, eszopiclone, and zopiclone (the last of which is not available in the United States). The adverse events and withdrawal symptoms of nonbenzodiazepine BZRAs were also assessed in a separate systematic review (41). On the basis of these reviews, benefits seemed to outweigh potential harms; however, the U.S. Food and Drug Administration recently released a safety announcement on the risk for serious injuries caused by sleep behaviors (sleepwalking, sleep driving, and other activities while not fully awake) associated with these

Figure 2. Module B: management of chronic insomnia disorder.



Sidebar 3: Components of Sleep Education, Overview of Behavioral Interventions, and Contraindications

Patient education and SDM:
- General information on insomnia disorder
- Education about behavioral treatment options
- Discussion of treatment options (risks, benefits, preferences, and alternatives)

Behavioral treatment components (CBT-I and BBT-I):
- Sleep restriction therapy: Limits time in bed to actual sleep duration to increase sleep drive; time in bed extended across treatment
- Stimulus control: Strengthens bed as a cue for sleep rather than wakefulness
- Relaxation: Reduces physiologic arousal and promotes optimal conditions for sleep
- Sleep hygiene education: Counseling on behaviors that interfere with sleep
- Cognitive restructuring (CBT-I only): Addresses cognitive arousal (busy or racing mind) by challenging unhelpful thoughts and beliefs about sleep, a natural result of the struggle with insomnia

Conditions requiring tailored or delayed CBT-I:
- Medical instability
- Active alcohol or drug use disorder
- Excessive daytime sleepiness
- Engagement in exposure-based PTSD treatment
- Uncontrolled seizure disorder
- Bipolar disorder
- Current acute mental health symptoms

Sidebar 4: Pharmacotherapy Considerations for Chronic Insomnia Disorder

Before starting short-term pharmacotherapy, review sleep history and evaluate contraindications for pharmacotherapy:
- Evaluate for other sleep disorders (e.g., apnea, NREM parasomnias), daytime sleepiness, respiratory impairment, cognitive impairment, substance abuse history, and medication interactions
- Encourage nonpharmacologic approaches (e.g., CBT-I or BBT-I)

When short-term pharmacotherapy is appropriate, consider the following:
- Low-dose doxepin; or
- Nonbenzodiazepine benzodiazepine receptor agonists (all patients offered these drugs should be specifically counseled on the risk for complex sleep-related behaviors)

The use of antipsychotic agents is ***not*** suggested for treatment of chronic insomnia disorder.

Consider sleep specialist referral in patients who do not respond to pharmacotherapy.

Sidebar 5: Other Approaches

CIH treatments suggested for chronic insomnia disorder:
- Auricular acupuncture with seed and pellet

Other treatments ***not*** suggested for chronic insomnia disorder:
- Alpha-Stim (Electromedical Products International)
- Cranial electrical stimulation
- Diphenhydramine
- Melatonin
- Chamomile
- Valerian

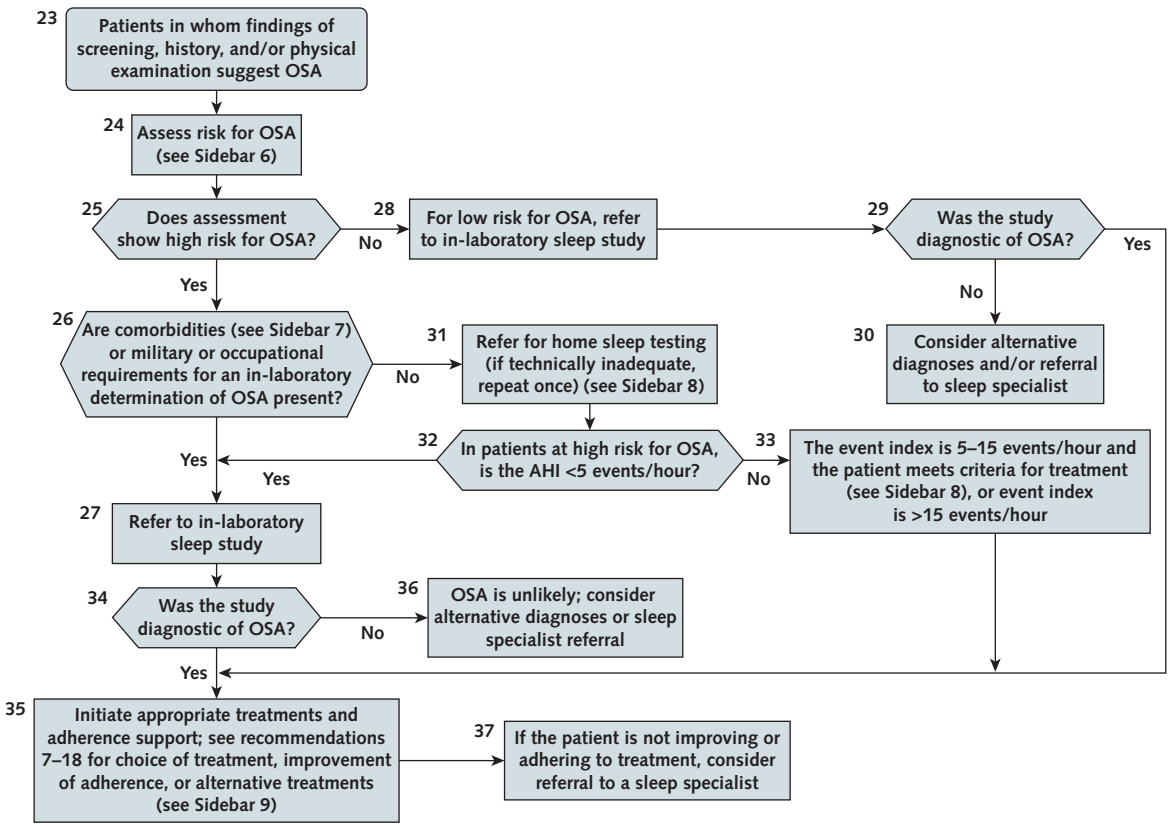
Other treatments ***not*** recommended for chronic insomnia disorder:
- Kava

BBT-I = brief behavioral therapy for insomnia; CBT-I = cognitive behavioral therapy for insomnia; CIH = complementary and integrative health; NREM = non-rapid eye movement; PTSD = posttraumatic stress disorder; SDM = shared decision making.

* In cases where the patient requires immediate intervention, providers may exercise clinical judgment to determine whether pharmacotherapy may be safely initiated.

† CBT-I and BBT-I are not equivalent, and there is more robust evidence for CBT-I. Although this algorithm uses CBT-I and BBT-I similarly, providers referring patients for these treatments should consider availability of the treatment, the complexity and comorbidities of the patient, and the training of the provider.

Figure 3. Module C: management of OSA.



Sidebar 6: Risk for OSA*

Consider using STOP questionnaire for risk stratification:
- Snoring loudly
- Tired, fatigue, sleepy in daytime
- Observed to stop breathing
- Treated for hypertension

High risk if patient answers "yes" to ≥2 items
Low risk if patient answers "yes" to <2 items

STOP questionnaire should not replace clinical judgment. Clinical assessment should include body mass index >30 kg/m^2, age >50 years, menopausal status, neck circumference, family history, and crowded oropharynx.

Sidebar 7: Comorbidities

Significant cardiorespiratory disease
- Cardiovascular comorbidities, including congestive heart failure
- Pulmonary comorbidities that affect baseline oxygen saturation or require oxygen therapy, including chronic obstructive pulmonary disease (GOLD stage III or IV)

Stroke
Respiratory muscle weakness
Hypoventilation/suspected hypoventilation due to neuromuscular or pulmonary disorder
Opioid use
Chronic insomnia
PTSD

Sidebar 8: AHI of 5–15 Events per Hour on HSAT

Treatment of OSA is recommended for symptomatic patients with an AHI or REI of 5–15 events per hour.
For patients who will have work and/or lifestyle limitations, definitive testing with in-laboratory PSG is recommended.
For the general population without work or lifestyle restrictions, an AHI of 5–15 events per hour on HSAT should be treated as OSA.

Sidebar 9: Treatment of OSA

For patients with severe OSA (i.e., AHI ≥30 events/h), the recommended initial therapy is PAP.
For patients with mild to moderate OSA (i.e., AHI 5–<30 events/h), PAP or MAD therapy can be considered initially. Choice of treatment should be based on clinical evaluation, comorbidities, and patient preference.
Educational, behavioral therapy, and supportive interventions should be offered to improve PAP adherence.
Weight loss and a comprehensive lifestyle intervention program should be encouraged in all patients with OSA who are overweight or obese. Although weight loss alone is typically insufficient as therapy for OSA, it may result in an improvement in AHI.
In patients with OSA who are not adherent to PAP and/or MAD therapy or have persistent symptoms despite adequate therapy, referral to a physician with expertise in sleep medicine is recommended.

AHI = apnea–hypopnea index; GOLD = Global Initiative for Chronic Obstructive Lung Disease; HSAT = home sleep apnea testing; MAD = mandibular advancement device; OSA = obstructive sleep apnea; PAP = positive airway pressure; PSG = polysomnography; PTSD = posttraumatic stress disorder; REI = respiratory event index.
* High risk for or high pretest probability of OSA.

agents (54). To minimize the incidence of adverse events, a nonbenzodiazepine BZRA, if prescribed, should be administered at the lowest effective dose and for the shortest possible duration, and all patients offered these agents should be counseled on the potential risks.

The work group advised against use of benzodiazepines or trazodone for treatment of chronic insomnia disorder. This recommendation was based on 4 fair-quality systematic reviews (55–58) that evaluated use of pharmacologic agents. In these reviews, benzodiazepines improved sleep efficiency, sleep onset latency, sleep quality, total sleep time, and wake after sleep onset compared with placebo. However, the widely known harms and adverse effects of benzodiazepines, including risk for dependency and diversion, falls and cognitive impairment in older patients, hypoventilation in patients with respiratory conditions (including sleep apnea and obesity hypoventilation), and neuromuscular diseases, were deemed to substantially outweigh the benefits.

A systematic review reported no differences in sleep efficiency or rate of discontinuation due to adverse events between trazodone (dose range, 50 to 150 mg before bedtime) and placebo in patients diagnosed with chronic insomnia (57). Although trazodone was more effective at improving subjective sleep quality, there were no differences in sleep onset latency, total sleep time, or wake after sleep onset (57). The review had several limitations, including studies of very short durations of therapy (mean, 1.7 weeks) and follow-up of only 1 to 4 weeks. The low-quality evidence supporting the efficacy of trazodone was outweighed by its adverse effect profile.

The work group also advised against use of antihistamines and antipsychotics for treatment of chronic insomnia disorder. These drugs are often used off label because of their sedating effects; however, the systematic evidence review conducted for this guideline did not identify any studies that met inclusion criteria for their use as interventions for chronic insomnia disorder. In fact, because of the antimuscarinic adverse effect profile of antihistamines, the 2019 Beers Criteria carry a strong recommendation to avoid these drugs in older adults (59). In addition, tolerance of the sedative effects of antihistamines has been noted after 3 to 4 days of continuous use, limiting their benefit even for short-term treatment of insomnia symptoms. Antipsychotics, most commonly quetiapine, have been used to treat insomnia disorder, but the evidence supporting their use is sparse and unclear, with small sample sizes and short treatment durations, thus making any determination of efficacy inconclusive. All antipsychotics, including low-dose quetiapine, are known to cause harms (60), including increased risk for death in elderly populations with dementia-related psychosis and increased suicidal tendencies in children, adolescents, and young adults (61).

Over-the-Counter Complementary and Integrative Health Treatments

Several herbal over-the-counter therapies were found to be ineffective for treatment of chronic insomnia disorder. The reviewed studies showed no benefit of using kava to treat chronic insomnia disorder compared with placebo, and there is a known risk for acute fatal liver toxicity with kava (62, 63). The work group noted that the U.S. Food and Drug Administration has warned health care providers and the public about the risk for acute liver damage and death associated with kava (62). Given these serious potential harms, the work group decided on a "strong against" recommendation for kava.

Use of valerian and chamomile for treatment of insomnia was also not supported by evidence. A systematic review by Leach and Page that included 14 trials evaluated the efficacy and safety of 3 herbal medicines (valerian, kava, and chamomile) for treatment of insomnia disorder and found no between-group differences in the critical outcomes of daytime functioning, insomnia severity, and sleep efficiency or the important outcomes of sleep onset latency, total sleep time, wake after sleep onset, and sleep quality with either valerian or chamomile (63). Specifically, no differences in either daytime functioning or insomnia severity were found for valerian or chamomile versus placebo.

The work group also did not find evidence to support use of melatonin for treatment of chronic insomnia disorder. The primary evidence base was a meta-analysis by Ferracioli-Oda and colleagues that included 19 studies of patients with primary insomnia (*Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition* criteria), with highly variable treatment durations and doses of melatonin in the included studies (64). The primary outcomes were reduction in sleep latency, increase in total sleep time, and overall improvement in sleep quality. The critical outcomes of daytime functioning and ISI scores were not assessed, and adverse events were not discussed. The evidence showed an approximately 7-minute decrease in sleep latency, an 8-minute increase in total sleep time, and a very small improvement in sleep quality; however, the clinical significance of these findings was unclear. A meta-regression analysis suggested that the trials with longer treatment durations and higher doses showed greater effects on sleep latency and total sleep time but did not improve sleep quality.

CONCLUSION

Using a systematic, evidence-based approach, the work group identified 41 recommendations (**Table**) related to the diagnosis and treatment of OSA and chronic insomnia disorder, with the goal of improving outcomes for patients receiving care through the VA and DoD health care systems. Clinical practice algorithms that can assist clinicians in assessing and managing patients with chronic insomnia disorder and OSA are provided in **Figures 1** to **3**. Evidence supports evaluation of sleep symptoms and timely diagnosis of these

2 disorders. In addition, the work group recommended specific treatments for OSA, particularly PAP therapy, with other options for patients who do not sufficiently benefit from this approach. The work group recommended CBT-I, which is supported by a large evidence base, for treatment of chronic insomnia disorder and also identified several other treatment options with emerging evidence supporting their use. Of note, the work group also recommended against several treatment approaches that are less effective (thereby diverting resources from other more effective treatments or limiting patient confidence in subsequent treatments) or that carry safety concerns. In all patients with sleep disorders, consultation with a sleep medicine specialist should be considered, especially for those in whom the diagnosis is uncertain or treatment proves challenging. Future research combining therapies for OSA and insomnia is needed, and comparative effectiveness trials evaluating the relative benefits of different approaches are warranted.

From University of Texas Health Science Center at San Antonio, San Antonio, Texas (V.M.); David Geffen School of Medicine at UCLA and VA Greater Los Angeles Healthcare System, Los Angeles, California (J.M.); Durham VA Healthcare System and Duke University School of Medicine, Durham, North Carolina (C.S.U.); John D. Dingell VA Medical Center Sleep Wake Disorders Center and Wayne State University, Detroit, Michigan (S.C.); U.S. Army SAMHS Sleep Medicine Service, San Antonio, Texas, and Wilford Hall Ambulatory Surgical Center, Lackland Air Force Base, Texas (M.S.B.); Walter Reed National Military Medical Center/Defense Health Agency, Bethesda, Maryland (C.S.); and Department of Veterans Affairs, Washington, DC (J.S.).

Financial Support: By the Durham Center of Innovation to Accelerate Discovery and Practice Transformation (CIN-13-410) at the Durham VA Healthcare System.

Disclosures: Dr. Mysliwiec reports personal fees from CPAP Medical outside the submitted work. Dr. Martin reports serving as a member of the board of directors of the American Academy of Sleep Medicine. Authors not named here have disclosed no conflicts of interest. Disclosures can also be viewed at www.acponline.org/authors/icmje/ConflictOfInterestForms.do?msNum=M19-3575.

Corresponding Author: James Sall, PhD, Department of Veterans Affairs, 811 Vermont Avenue NW, Washington, DC 20420.

Current author addresses and author contributions are available at Annals.org.

References

1. **National Center on Sleep Disorders Research.** National Institutes of Health Sleep Disorders Research Plan. NIH publication no. 11-7820. Washington, DC: National Institutes of Health; November 2011. Accessed at www.nhlbi.nih.gov/files/docs/resources/sleep/201101011NationalSleepDisordersResearchPlanDHHSPublication11-7820.pdf on 7 January 2020.

2. **National Institutes of Health.** National Institutes of Health State of the Science Conference statement on manifestations and management of chronic insomnia in adults, June 13–15, 2005. Sleep. 2005;28:1049-57. [PMID: 16268373]

3. **Ford ES, Cunningham TJ, Giles WH, et al.** Trends in insomnia and excessive daytime sleepiness among U.S. adults from 2002 to 2012. Sleep Med. 2015;16:372-8. [PMID: 25747141] doi:10.1016/j.sleep.2014.12.008

4. **Ohayon MM.** Epidemiology of insomnia: what we know and what we still need to learn. Sleep Med Rev. 2002;6:97-111. [PMID: 12531146]

5. **Morin CM, Benca R.** Chronic insomnia. Lancet. 2012;379:1129-41. [PMID: 22265700] doi:10.1016/S0140-6736(11)60750-2

6. **Senaratna CV, Perret JL, Lodge CJ, et al.** Prevalence of obstructive sleep apnea in the general population: a systematic review. Sleep Med Rev. 2017;34:70-81. [PMID: 27568340] doi:10.1016/j.smrv.2016.07.002

7. **Troxel WM, Shih RA, Pedersen ER, et al.** Sleep in the military: promoting healthy sleep among U.S. servicemembers. Rand Health Q. 2015;5:19. [PMID: 28083395]

8. **Taylor DJ, Pruiksma KE, Hale WJ, et al; STRONG STAR Consortium.** Prevalence, correlates, and predictors of insomnia in the US Army prior to deployment. Sleep. 2016;39:1795-806. [PMID: 27450687]

9. **Caldwell JA, Knapik JJ, Shing TL, et al.** The association of insomnia and sleep apnea with deployment and combat exposure in the entire population of US Army soldiers from 1997 to 2011: a retrospective cohort investigation. Sleep. 2019;42. [PMID: 31106808] doi:10.1093/sleep/zsz112

10. **Mysliwiec V, McGraw L, Pierce R, et al.** Sleep disorders and associated medical comorbidities in active duty military personnel. Sleep. 2013;36:167-74. [PMID: 23372263] doi:10.5665/sleep.2364

11. **Mysliwiec V, Gill J, Lee H, et al.** Sleep disorders in US military personnel: a high rate of comorbid insomnia and obstructive sleep apnea. Chest. 2013;144:549-57. [PMID: 23681455] doi:10.1378/chest.13-0088

12. **Foster SN, Hansen SL, Capener DC, et al.** Gender differences in sleep disorders in the US military. Sleep Health. 2017;3:336-41. [PMID: 28923189] doi:10.1016/j.sleh.2017.07.015

13. **Collen J, Orr N, Lettieri CJ, et al.** Sleep disturbances among soldiers with combat-related traumatic brain injury. Chest. 2012;142:622-30. [PMID: 22459784] doi:10.1378/chest.11-1603

14. **Martin JL, Schweizer CA, Hughes JM, et al.** Estimated prevalence of insomnia among women veterans: results of a postal survey. Womens Health Issues. 2017;27:366-73. [PMID: 28110799] doi:10.1016/j.whi.2016.12.003

15. **Alexander M, Ray MA, Hébert JR, et al.** The National Veteran Sleep Disorder Study: descriptive epidemiology and secular trends, 2000–2010. Sleep. 2016;39:1399-410. [PMID: 27091538] doi:10.5665/sleep.5972

16. **Zhang Y, Weed JG, Ren R, et al.** Prevalence of obstructive sleep apnea in patients with posttraumatic stress disorder and its impact on adherence to continuous positive airway pressure therapy: a meta-analysis. Sleep Med. 2017;36:125-32. [PMID: 28735910] doi:10.1016/j.sleep.2017.04.020

17. **Jenkins MM, Colvonen PJ, Norman SB, et al.** Prevalence and mental health correlates of insomnia in first-encounter veterans with and without military sexual trauma. Sleep. 2015;38:1547-54. [PMID: 26085301] doi:10.5665/sleep.5044

18. **Araújo T, Jarrin DC, Leanza Y, et al.** Qualitative studies of insomnia: current state of knowledge in the field. Sleep Med Rev. 2017;31:58-69. [PMID: 27090821] doi:10.1016/j.smrv.2016.01.003

19. **Ulmer CS, Bosworth HB, Beckham JC, et al.** Veterans Affairs primary care provider perceptions of insomnia treatment. J Clin Sleep Med. 2017;13:991-9. [PMID: 28728623] doi:10.5664/jcsm.6702

20. **Baldwin CM, Bell IR, Guerra S, et al.** Obstructive sleep apnea and ischemic heart disease in southwestern US veterans: implications for clinical practice. Sleep Breath. 2005;9:111-8. [PMID: 16091955]

21. **Bravata DM, McClain V, Austin C, et al.** Diagnosing and managing sleep apnea in patients with chronic cerebrovascular disease: a

randomized trial of a home-based strategy. Sleep Breath. 2017;21: 713-25. [PMID: 28386781] doi:10.1007/s11325-017-1494-5
22. **Graham R, Mancher M, Miller Wolman D, et al, eds.** Clinical Practice Guidelines We Can Trust. Washington, DC: National Academies Pr; 2011.
23. **Atkins D, Best D, Briss PA, et al; GRADE Working Group.** Grading quality of evidence and strength of recommendations. BMJ. 2004;328:1490. [PMID: 15205295]
24. **Andrews J, Guyatt G, Oxman AD, et al.** GRADE guidelines: 14. Going from evidence to recommendations: the significance and presentation of recommendations. J Clin Epidemiol. 2013;66:719-25. [PMID: 23312392] doi:10.1016/j.jclinepi.2012.03.013
25. **Andrews JC, Schünemann HJ, Oxman AD, et al.** GRADE guidelines: 15. Going from evidence to recommendation–determinants of a recommendation's direction and strength. J Clin Epidemiol. 2013; 66:726-35. [PMID: 23570745] doi:10.1016/j.jclinepi.2013.02.003
26. **Chiu HY, Chen PY, Chuang LP, et al.** Diagnostic accuracy of the Berlin Questionnaire, STOP-BANG, STOP, and Epworth Sleepiness Scale in detecting obstructive sleep apnea: a bivariate meta-analysis. Sleep Med Rev. 2017;36:57-70. [PMID: 27919588] doi:10.1016/j.smrv .2016.10.004
27. **Chung F, Yegneswaran B, Liao P, et al.** STOP questionnaire: a tool to screen patients for obstructive sleep apnea. Anesthesiology. 2008;108: 812-21. [PMID: 18431116] doi:10.1097/ALN.0b013e31816d83e4
28. **Rosen IM, Kirsch DB, Chervin RD, et al; American Academy of Sleep Medicine Board of Directors.** Clinical use of a home sleep apnea test: an American Academy of Sleep Medicine position statement. J Clin Sleep Med. 2017;13:1205-7. [PMID: 28942762] doi:10 .5664/jcsm.6774
29. **Barbé F, Durán-Cantolla J, Sánchez-de-la-Torre M, et al; Spanish Sleep And Breathing Network.** Effect of continuous positive airway pressure on the incidence of hypertension and cardiovascular events in nonsleepy patients with obstructive sleep apnea: a randomized controlled trial. JAMA. 2012;307:2161-8. [PMID: 22618923] doi:10 .1001/jama.2012.4366
30. **Soldatos CR, Dikeos DG, Paparrigopoulos TJ.** Athens Insomnia Scale: validation of an instrument based on ICD-10 criteria. J Psychosom Res. 2000;48:555-60. [PMID: 11033374]
31. **Chiu HY, Chang LY, Hsieh YJ, et al.** A meta-analysis of diagnostic accuracy of three screening tools for insomnia. J Psychosom Res. 2016;87:85-92. [PMID: 27411756] doi:10.1016/j.jpsychores.2016.06 .010
32. **Wozniak DR, Lasserson TJ, Smith I.** Educational, supportive and behavioural interventions to improve usage of continuous positive airway pressure machines in adults with obstructive sleep apnoea. Cochrane Database Syst Rev. 2014:CD007736. [PMID: 24399660] doi:10.1002/14651858.CD007736.pub2
33. **Khan SU, Duran CA, Rahman H, et al.** A meta-analysis of continuous positive airway pressure therapy in prevention of cardiovascular events in patients with obstructive sleep apnoea. Eur Heart J. 2018;39:2291-7. [PMID: 29069399] doi:10.1093/eurheartj/ehx597
34. **Zhao YY, Wang R, Gleason KJ, et al; BestAIR Investigators.** Effect of continuous positive airway pressure treatment on health-related quality of life and sleepiness in high cardiovascular risk individuals with sleep apnea: Best Apnea Interventions for Research (BestAIR) trial. Sleep. 2017;40. [PMID: 28419387] doi:10.1093/sleep/zsx040
35. **Bastos HN, Cardoso AV, Castro AS, et al.** Randomised short-term trial of high-span versus low-span APAP for treating sleep apnoea. Sleep Breath. 2016;20:183-90. [PMID: 26066701] doi:10.1007 /s11325-015-1203-1
36. **El-Solh AA, Homish GG, Ditursi G, et al.** A randomized crossover trial evaluating continuous positive airway pressure versus mandibular advancement device on health outcomes in veterans with posttraumatic stress disorder. J Clin Sleep Med. 2017;13:1327-35. [PMID: 29065960] doi:10.5664/jcsm.6808
37. **Schwartz M, Acosta L, Hung YL, et al.** Effects of CPAP and mandibular advancement device treatment in obstructive sleep apnea patients: a systematic review and meta-analysis. Sleep Breath. 2018; 22:555-68. [PMID: 29129030] doi:10.1007/s11325-017-1590-6
38. **Banhiran W, Assanasen P, Nopmaneejumrudlers C, et al.** Adjustable thermoplastic oral appliance versus positive airway pressure for obstructive sleep apnea. Laryngoscope. 2018;128:516-22. [PMID: 28714534] doi:10.1002/lary.26753
39. **Nikolopoulou M, Byraki A, Ahlberg J, et al.** Oral appliance therapy versus nasal continuous positive airway pressure in obstructive sleep apnoea syndrome: a randomised, placebo-controlled trial on self-reported symptoms of common sleep disorders and sleep-related problems. J Oral Rehabil. 2017;44:452-60. [PMID: 28294380] doi:10.1111/joor.12505
40. **de Vries GE, Wijkstra PJ, Houwerzijl EJ, et al.** Cardiovascular effects of oral appliance therapy in obstructive sleep apnea: a systematic review and meta-analysis. Sleep Med Rev. 2018;40:55-68. [PMID: 29195726] doi:10.1016/j.smrv.2017.10.004
41. **Brasure M, MacDonald R, Fuchs E, et al.** Management of Insomnia Disorder. Comparative Effectiveness Reviews no. 159. Report no. 15(16)-EHC027-EF. Rockville, MD: Agency for Healthcare Research and Quality; 2015.
42. **Buysse DJ.** Insomnia. JAMA. 2013;309:706-16. [PMID: 23423416] doi:10.1001/jama.2013.193
43. **Johnson JA, Rash JA, Campbell TS, et al.** A systematic review and meta-analysis of randomized controlled trials of cognitive behavior therapy for insomnia (CBT-I) in cancer survivors. Sleep Med Rev. 2016;27:20-8. [PMID: 26434673] doi:10.1016/j.smrv.2015.07.001
44. **Taylor DJ, Peterson AL, Pruiksma KE, et al; STRONG STAR Consortium.** Internet and in-person cognitive behavioral therapy for insomnia in military personnel: a randomized clinical trial. Sleep. 2017; 40. [PMID: 28472528] doi:10.1093/sleep/zsx075
45. **Laurel Franklin C, Walton JL, Raines AM, et al.** Pilot study comparing telephone to in-person delivery of cognitive-behavioural therapy for trauma-related insomnia for rural veterans. J Telemed Telecare. 2018; 24:629-35. [PMID: 28950755] doi:10.1177/1357633X17732366
46. **Lancee J, van Straten A, Morina N, et al.** Guided online or face-to-face cognitive behavioral treatment for insomnia: a randomized wait-list controlled trial. Sleep. 2016;39:183-91. [PMID: 26414893] doi:10.5665/sleep.5344
47. **Blom K, Tarkian Tillgren H, Wiklund T, et al.** Internet-vs. group-delivered cognitive behavior therapy for insomnia: a randomized controlled non-inferiority trial. Behav Res Ther. 2015;70:47-55. [PMID: 25981329] doi:10.1016/j.brat.2015.05.002
48. **Espie CA, Kyle SD, Williams C, et al.** A randomized, placebo-controlled trial of online cognitive behavioral therapy for chronic insomnia disorder delivered via an automated media-rich web application. Sleep. 2012;35:769-81. [PMID: 22654196] doi:10.5665/sleep .1872
49. **Chung KF, Lee CT, Yeung WF, et al.** Sleep hygiene education as a treatment of insomnia: a systematic review and meta-analysis. Fam Pract. 2018;35:365-75. [PMID: 29194467] doi:10.1093/fampra /cmx122
50. **Morgan K, Gregory P, Tomeny M, et al.** Self-help treatment for insomnia symptoms associated with chronic conditions in older adults: a randomized controlled trial. J Am Geriatr Soc. 2012;60: 1803-10. [PMID: 23035962] doi:10.1111/j.1532-5415.2012.04175.x
51. **Mitchell MD, Gehrman P, Perlis M, et al.** Comparative effectiveness of cognitive behavioral therapy for insomnia: a systematic review. BMC Fam Pract. 2012;13:40. [PMID: 22631616] doi:10.1186/ 1471-2296-13-40
52. **Yeung WF, Chung KF, Yung KP, et al.** Doxepin for insomnia: a systematic review of randomized placebo-controlled trials. Sleep Med Rev. 2015;19:75-83. [PMID: 25047681] doi:10.1016/j.smrv.2014 .06.001
53. **Mansbach RS, Ludington E, Rogowski R, et al.** A placebo- and active-controlled assessment of 6- and 50-mg oral doxepin on cardiac repolarization in healthy volunteers: a thorough QT evaluation. Clin Ther. 2011;33:851-62. [PMID: 21722958] doi:10.1016/j.clinthera .2011.05.092
54. **U.S. Food and Drug Administration.** FDA adds boxed warning for risk of serious injuries caused by sleepwalking with certain prescription insomnia medicines. 30 April 2019. Accessed at www.fda .gov/drugs/drug-safety-and-availability/fda-adds-boxed-warning-risk-

serious-injuries-caused-sleepwalking-certain-prescription-insomnia on 31 July 2019.
55. **Winkler A, Auer C, Doering BK, et al.** Drug treatment of primary insomnia: a meta-analysis of polysomnographic randomized controlled trials. CNS Drugs. 2014;28:799-816. [PMID: 25168785] doi:10.1007/s40263-014-0198-7
56. **Kuriyama A, Honda M, Hayashino Y.** Ramelteon for the treatment of insomnia in adults: a systematic review and meta-analysis. Sleep Med. 2014;15:385-92. [PMID: 24656909] doi:10.1016/j.sleep.2013.11.788
57. **Yi XY, Ni SF, Ghadami MR, et al.** Trazodone for the treatment of insomnia: a meta-analysis of randomized placebo-controlled trials. Sleep Med. 2018;45:25-32. [PMID: 29680424] doi:10.1016/j.sleep.2018.01.010
58. **Liu Y, Xu X, Dong M, et al.** Treatment of insomnia with tricyclic antidepressants: a meta-analysis of polysomnographic randomized controlled trials. Sleep Med. 2017;34:126-33. [PMID: 28522080] doi:10.1016/j.sleep.2017.03.007
59. **By the 2019 American Geriatrics Society Beers Criteria® Update Expert Panel.** American Geriatrics Society 2019 updated AGS Beers Criteria® for potentially inappropriate medication use in older adults. J Am Geriatr Soc. 2019;67:674-94. [PMID: 30693946] doi:10.1111/jgs.15767
60. **Coe HV, Hong IS.** Safety of low doses of quetiapine when used for insomnia. Ann Pharmacother. 2012;46:718-22. [PMID: 22510671] doi:10.1345/aph.1Q697
61. **U.S. Food and Drug Administration.** Full Prescribing Information: Seroquel. 2017. Accessed at www.accessdata.fda.gov/drugsatfda_docs/label/2017/020639s065lbl.pdf on 31 July 2019.
62. **U.S. Food and Drug Administration.** Consumer Advisory: Kava-Containing Dietary Supplements May Be Associated With Severe Liver Injury. 2002. Accessed at https://nccih.nih.gov/news/alerts/kava on 20 November 2018.
63. **Leach MJ, Page AT.** Herbal medicine for insomnia: a systematic review and meta-analysis. Sleep Med Rev. 2015;24:1-12. [PMID: 25644982] doi:10.1016/j.smrv.2014.12.003
64. **Ferracioli-Oda E, Qawasmi A, Bloch MH.** Meta-analysis: melatonin for the treatment of primary sleep disorders. PLoS One. 2013;8:e63773. [PMID: 23691095] doi:10.1371/journal.pone.0063773

Current Author Addresses: Dr. Mysliwiec: Department of Psychiatry and Behavioral Sciences, University of Texas Health Science Center at San Antonio, 7703 Floyd Curl Drive, MC 7747, San Antonio, TX 78229-3900.
Dr. Martin: VA Greater Los Angeles Healthcare System, VA Sepulveda GRECC, 16111 Plummer Street (11E), North Hills, CA 91343.
Dr. Ulmer: Health Services Research & Development (HSR&D) (152), Durham VA Healthcare System, 508 Fulton Street, Durham, NC 27705.
Dr. Chowdhuri: John D. Dingell VA Sleep Wake Disorders Center, Medical Service, 4646 John R Street (11M), Detroit, MI 48201.
Dr. Brock: U.S. Air Force SAMHS Sleep Medicine Service, Wilford Hall Ambulatory Surgical Center, 1100 Wilford Hall Loop, Lackland AFB, TX 78236.
Dr. Spevak: Walter Reed National Military Medical Center/Defense Health Agency, 8901 Rockville Pike, Bethesda, MD 20889.
Dr. Sall: Evidence-Based Practice Program, Office of Quality, Safety and Value (10E2B), Department of Veterans Affairs, 811 Vermont Avenue, NW, Washington, DC 20420.

Author Contributions: Conception and design: V. Mysliwiec, J. Martin, C.S. Ulmer, S. Chowdhuri, C. Spevak.
Analysis and interpretation of the data: J. Martin, C.S. Ulmer.
Drafting of the article: V. Mysliwiec, J. Martin, C.S. Ulmer, S. Chowdhuri, M.S. Brock, C. Spevak, J. Sall.
Critical revision of the article for important intellectual content: V. Mysliwiec, J. Martin, S. Chowdhuri, M.S. Brock, C. Spevak, J. Sall.
Final approval of the article: V. Mysliwiec, J. Martin, C.S. Ulmer, S. Chowdhuri, M.S. Brock, C. Spevak, J. Sall.
Administrative, technical, or logistic support: M.S. Brock, J. Sall.
Collection and assembly of data: J. Martin, M.S. Brock.